Breast cancer is a leading cause of cancer death of women in the U.S. today. Members of the family of insulin-like growth factors (IGFs) are proposed to play a major role in the development and subsequent uncontrolled proliferation of breast cancer cells. Insulin-like growth factor-I (IGF-I) is known to be a potent mitogen for mammary epithelial cells. IGF-I acts by binding to cell surface receptors, thereby stimulating a cascade of events leading to cell division. In the interest of interrupting the effect of IGF-I on cancerous mammary epithelial cells, an understanding of how IGF-I behaves in the presence of other extracellular components is needed. This study examines the IGF-I response of SV40-IGF-I, an immortalized bovine mammary epithelial cell line which secretes IGF-I constitutively.

The microphysiometer allows real-time sampling of cellular activity by measuring the excretion of protons from a sample of cells stimulated by IGF-I binding. The contributions of other factors in enhancing or suppressing stimulation can be compared by examining the pH response of cells exposed to IGF-I in the presence of these factors. We present data showing the stimulatory effect of IGF-I in a dose dependent manner on the SV40-IGF-I cell line.

In addition, we compare IGF-I stimulation with stimulation by long R’IGF-I, a substituted analogue of IGF-I having a reduced binding affinity for the IGF binding proteins. We examine the effect of insulin-like binding protein-3 (IGFBP-3) both in the presence and absence of IGF-I, finding no IGF-I independent effect in the rapid binding experiment and no effect on stimulation of IGFBP-3 pre-incubated cells by subsequent IGF-I challenge. This is of particular interest due to recent work demonstrating an IGF-
independent IGFBP-3 response in a number of cell lines. Binding studies to correlate
with the rapid binding stimulation show binding of the IGFBP-3 molecule with high
affinity to a small number of surface receptors on the SV40-IGF-I cell.

Analysis of the extracellular environment and the components contributing to the binding
of IGF-I to the cell membrane receptor will provide information for the development of
interventions to slow or interrupt the process of IGF-I binding and therefore cancer
growth. Optimization of the Cytosensor® Microphysiometer System for the (transfected)
SV40-IGF-I and the (parental) MAC-T cell lines was achieved to continue comparison
studies of autocrine and paracrine stimulation of bovine mammary epithelial cells by
IGF-I.